

The Reactions of 4-Dicyanomethylene-2-phenyl-4*H*-1-benzopyran and Some Benzologs with Nucleophiles

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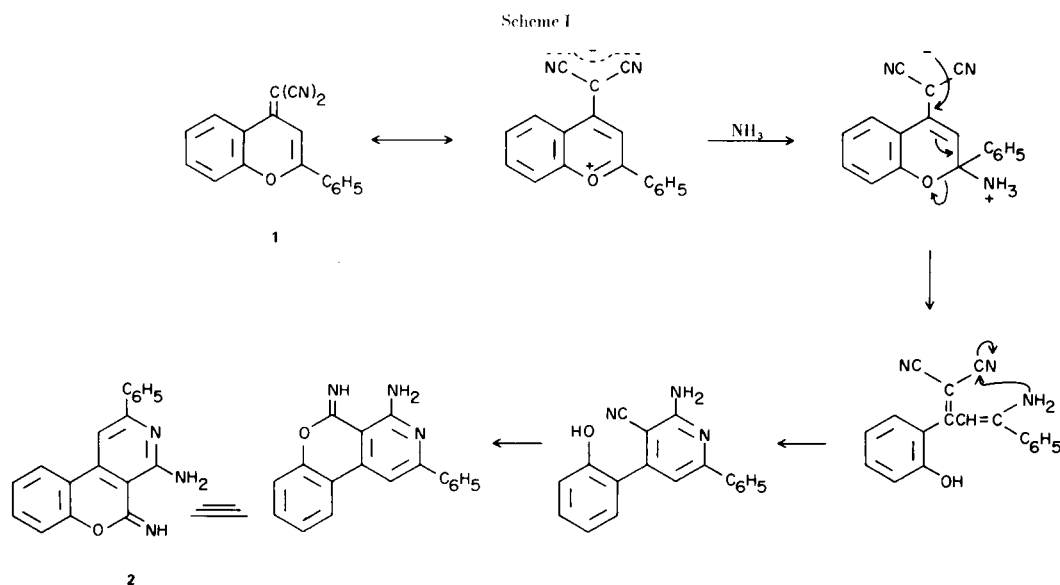
4-Dicyanomethylene-2-phenyl-4*H*-1-benzopyran (**1**) reacts with primary amines under mild conditions to give 4-imino-3-alkyl-5-alkylimino-2-phenyl-3,4-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine derivatives which, in turn, are hydrolyzed with acid to 4-imino-3-alkyl-2-phenyl-3,4-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-ones. When more vigorous conditions are employed for the reactions of **1** with primary amines, Dimroth rearrangements take place and the products are derivatives of 4-alkyl- (or aryl)amino-5-alkyl- (or aryl)imino-2-phenyl-5*H*-[1]benzopyrano[3,4-*c*]pyridine. The latter compounds are hydrolyzed by acid to the corresponding 5-pyridone derivatives. The reaction of **1** with piperidine gives 2-phenyl-4-piperidyl-5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-one. Sodium methoxide reacts with **1** to give 3-cyano-2-methoxy-4-(2-hydroxyphenyl)-6-phenylpyridine. Two benzologs of **1** have been allowed to react with primary and secondary amines and the products are analogous to those obtained from **1**.

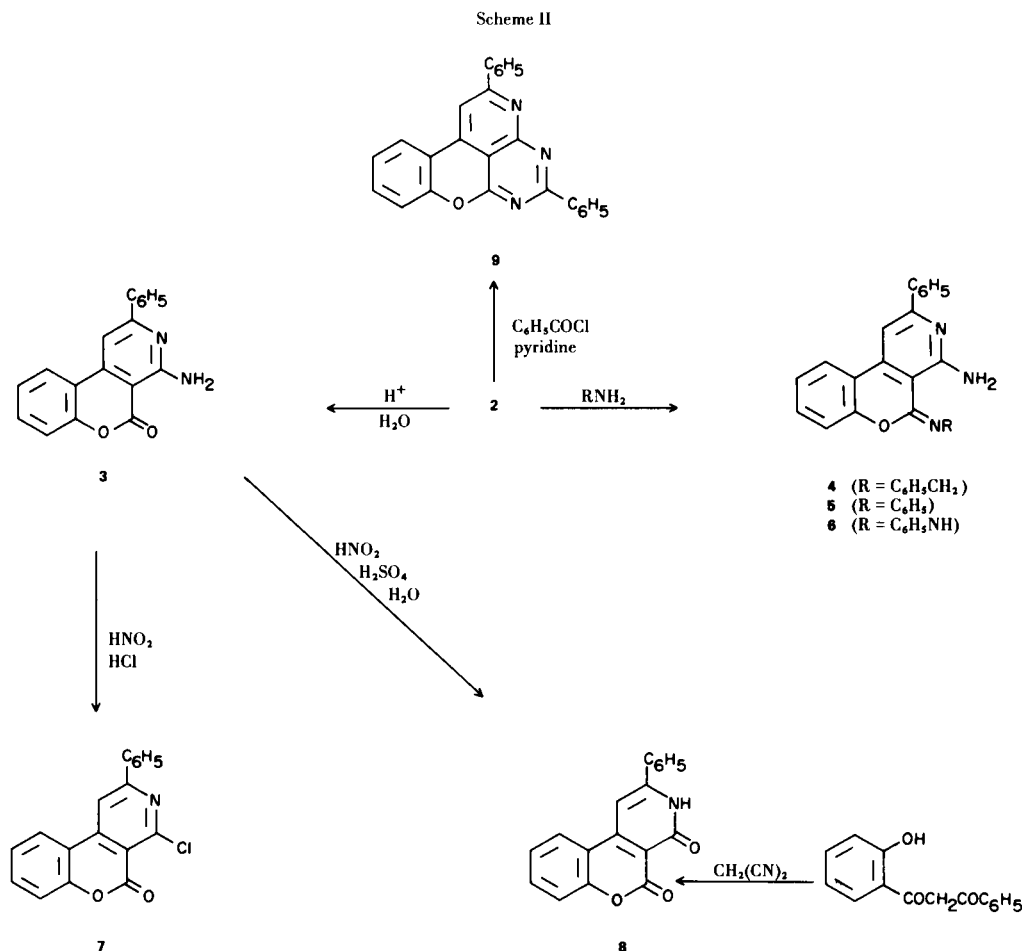
The reactions of 4-dicyanomethylene-4*H*-pyrans with primary and secondary amines have been reported (1). The present paper describes some reactions of 4-dicyanomethylene-2-phenyl-4*H*-1-benzopyran (**1**) and several of its benzo-homologs with ammonia, primary and secondary amines, and several other nucleophiles.

We have ascribed the reactivity of the dicyanomethylenepyran toward amines to their pyrylium character (1). It has been reported that benzopyrylium salts do not react with amines to give pyridine compounds (2), and it was therefore of interest to find that **1**

reacts readily with ammonia and amines to give pyridine derivatives. However, we believe that these reactions are not comparable, since **1** reacts with the amines by a completely different reaction path from that which would be predicted for the reaction of amines with benzopyrylium salts and, therefore, the difference in the behavior of these compounds does not exclude the pyryliumlike nature of **1**.

Compound **1** reacts with concentrated ammonium hydroxide in refluxing pyridine to give a compound to which was assigned the structure **2**. A reaction scheme, which is





similar to that proposed for the reaction of 4-dicyanomethylene-4*H*-pyrans with amines (1), is shown in Scheme I.

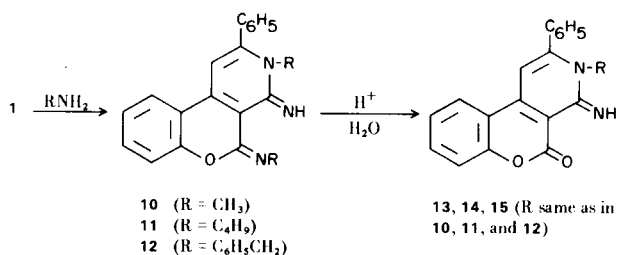
The imino group of **2** is hydrolyzed on treatment with aqueous mineral acids to give **3** and is readily replaced by other amines such as benzylamine, aniline, and phenylhydrazine to give **4**, **5**, and **6**, respectively. Treatment of **3** with sodium nitrite in hydrochloric acid results in the replacement of the amino group by chlorine to give **7**, and the use of sulfuric acid in place of the hydrochloric acid gives the pyridone **8**, which was also prepared from 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione and malononitrile. The reaction of malononitrile with this *o*-hydroxydiketone to give **8** was based on the known reactions of malononitrile with *o*-hydroxyketones and with β -diketones (3). Compound **2** can also be used to prepare more complex heterocyclics, as illustrated by the formation of **9** from **2** and benzoyl chloride in pyridine.

Compound **1** reacts with methylamine in refluxing pyridine, with refluxing butylamine, and with benzylamine at 80-90° to give the diimino compounds **10**, **11**,

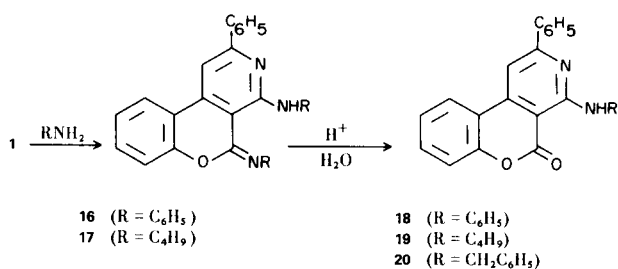
and **12**, respectively. Compounds **11** and **12** were oils which did not crystallize, but the mass spectra of the oils verified the assigned structures. The diimino compounds were hydrolyzed with acid to the crystalline lactones **13**, **14**, and **15**.

When the reactions of **1** and primary amines were carried out at elevated temperatures, the products were isomers of the diimines and were formed by Dimroth rearrangements (4) of the diimines. For example, **1** reacted with refluxing aniline, or with butylamine in a bomb at 150°, to give the aminopyridine derivatives **16** and **17** (Scheme IV), which were in turn hydrolyzed by acid to **18** and **19**. Refluxing a solution of **1** in benzylamine led to the formation of a mixture of noncrystalline products, which were hydrolyzed with acid to give **3** and **20**. We ascribe the formation of **3** to the ammonia which is generated when benzylamine is refluxed. Another example involving the reaction of ammonia which is liberated from benzylamine is given in Scheme VII. The occurrence of a Dimroth rearrangement was demonstrated by the rearrangement of **14** to give **19** in either

Scheme III



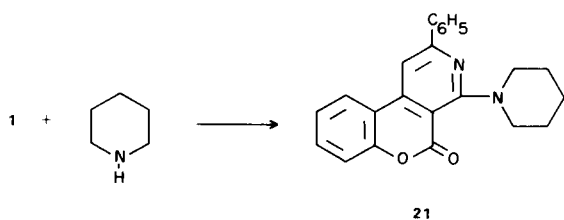
Scheme IV



refluxing benzylamine or a refluxing solution of potassium hydroxide in ethoxyethanol. The rearrangement is not very facile since potassium hydroxide in refluxing methyl alcohol did not cause any rearrangement to take place. The mechanism for the rearrangement should be similar to that which we have proposed for a related series of iminopyridine derivatives (1). Another example of the rearrangement occurs when **15** is heated in benzylamine to give **20**.

Secondary amines react with **1** to give aminopyridone derivatives, as would be expected from the results obtained with 4-dicyanomethylene-4*H*-pyrans (1). For example, piperidine and **1** gave the aminopyridine derivative **21**. It is likely that a 5-iminium derivative is the primary product, but hydrolysis to give **21** occurs during the recrystallization from aqueous acetic acid.

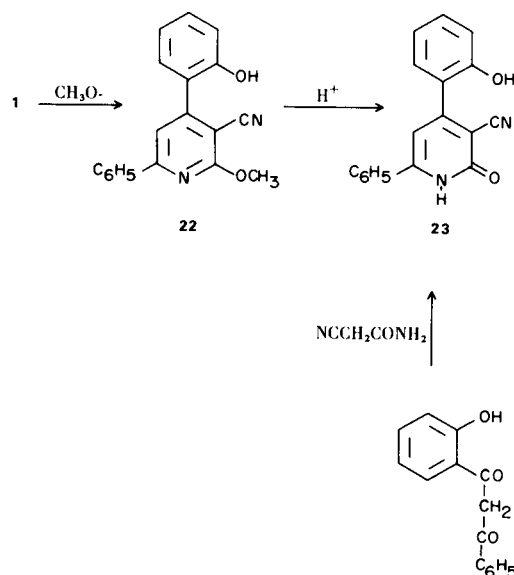
Scheme V



The reaction of **1** with sodium methoxide in methyl alcohol gave a compound which is tentatively assigned structure **22** (Scheme VI). The absorption data and the fact that acid hydrolysis gave the pyridone **23** support the assigned structure, but the fact that cyclization has not

taken place between the cyano and hydroxy groups is not consistent with the other examples described in this paper. The pyridone **23** was also prepared from 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione and cyanoacetamide.

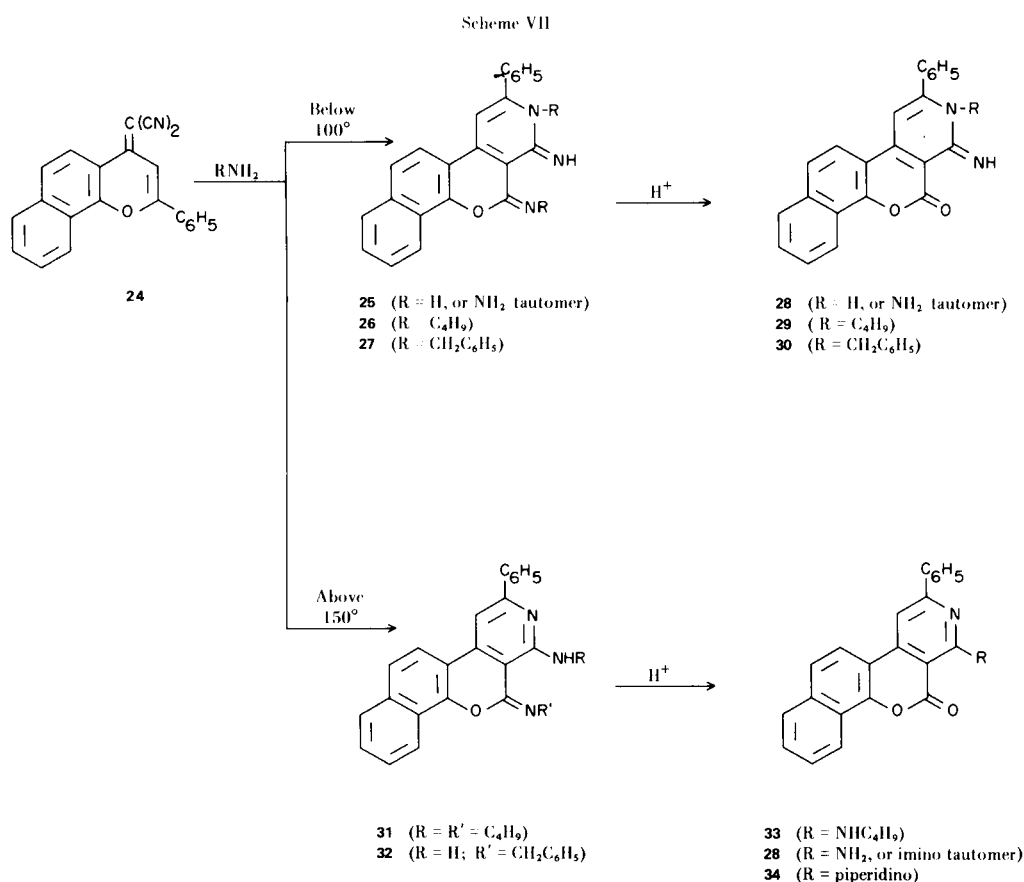
Scheme VI



We have examined the reactions of two benzologs of **1** with amines. For example, **24** reacted with primary amines at lower temperatures to give diimino derivatives and at higher temperatures to yield products which are derived from Dimroth rearrangements of the diimines. Some examples are shown in Scheme VII, and it can be seen that they are entirely analogous to the corresponding reactions with **1**. Piperidine reacts with **24** to give **34**.

Cyanoacetamide or cyanoacetanilide reacted with **24** in the presence of potassium hydroxide to give a product which has been assigned structure **35**. A reasonable reaction sequence is given in Scheme VIII. The adjacency of the imino and amino groups is demonstrated by the formation of **36**. Acid hydrolysis of the imino group gave the lactone **37**.

The other benzolog of **1** that has been briefly investigated is **38**. The reaction of **38** with refluxing butylamine followed by acid hydrolysis gave the imino derivative **39**. However, a repeat under slightly different conditions resulted in the formation of the aminopyridine derivative **40**. We think that both isomers are formed in this reaction and that the change in the experimental conditions affects the isolation of the products. Piperidine reacts with **38** to give compound **41**, which did not show a lactone band in the ir spectrum, but did show bands characteristic of the cyano and hydroxy groups.



The aminopyridine and iminopyridine isomers described in this paper are readily distinguishable on the basis of the mass spectral cracking patterns and the electronic and nmr spectra. The iminopyridine isomers always showed a large *m/e* for M-H, and the aminopyridine isomers either did not show this mass or the amount was small. The iminopyridine isomers showed long wavelength electronic absorptions at substantially longer wavelengths than the aminopyridine compounds. The two classes of compounds were also readily identified by their nmr spectra, since the signal for the proton in the 1-position was in the vinyl region in the case of the iminopyridines and in the aromatic region for the aminopyridines.

EXPERIMENTAL (5)

4-Dicyanomethylene-2-phenyl-4H-1-benzopyran (1).

Compound 1 was prepared from 4-flavone and malononitrile or from 4-methoxyflavylium perchlorate and malononitrile by the procedures which have been described previously for 4-pyrones (6). Compound 1 melted at 175-176° (reported (7), m.p. 178-180°).

The λ max ($\epsilon \times 10^{-3}$) are 236 (18.2), 313 (18.0) and 398 μ (25.0).

4-Amino-5-imino-2-phenyl-4H-[1]benzopyrano[3,4-c]pyridine (2).

A solution of 2.7 g. of 1 in 50 ml. of pyridine was heated to reflux and 10 ml. of ammonium hydroxide was added. The mixture was refluxed for 15 minutes, cooled, and the solid was collected and crystallized from ethoxyethanol, yielding 2.5 g. of 2, m.p. 201-203°.

The λ max ($\epsilon \times 10^{-3}$) are 259 (35.3), 325 (7.4), and 365 μ (12.8).

Anal. Calcd. for C₁₈H₁₃N₃O: C, 75.2; H, 4.6; N, 14.6. Found: C, 75.0; H, 4.4; N, 14.7.

4-Amino-2-phenyl-5H-[1]benzopyrano[3,4-c]pyridin-5-one (3).

A mixture of 2 g. of 2, 20 ml. of acetic acid, and 2 ml. of concentrated hydrochloric acid was refluxed for 2 hours, diluted with water, and the solid was collected and crystallized from pyridine, yielding 2 g. of 3, m.p. 210-211°.

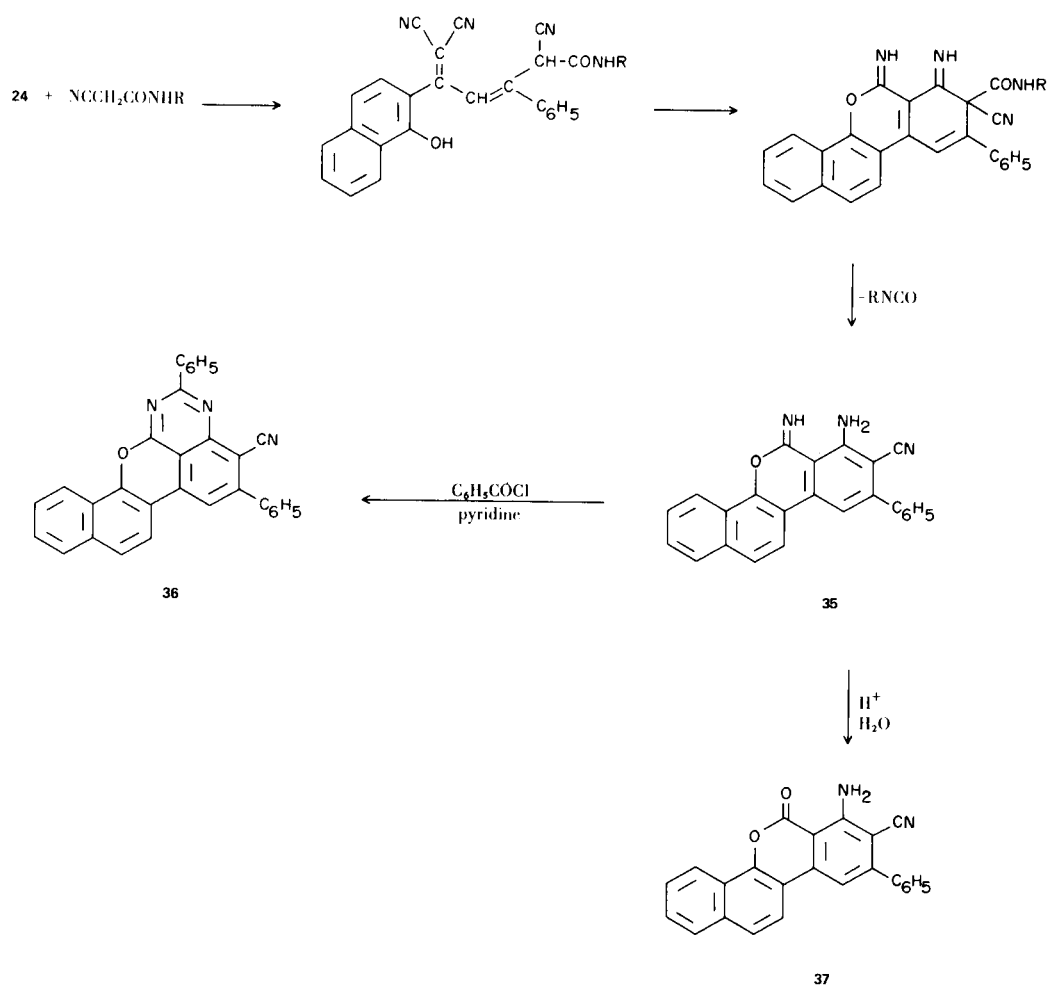
The λ max ($\epsilon \times 10^{-3}$) are 257 (31.8), 315 (2.67), and 373 μ (14.7).

Compound 3 shows absorption at 5.9 μ for the carbonyl and at 2.88 and 3 μ for the primary amino group.

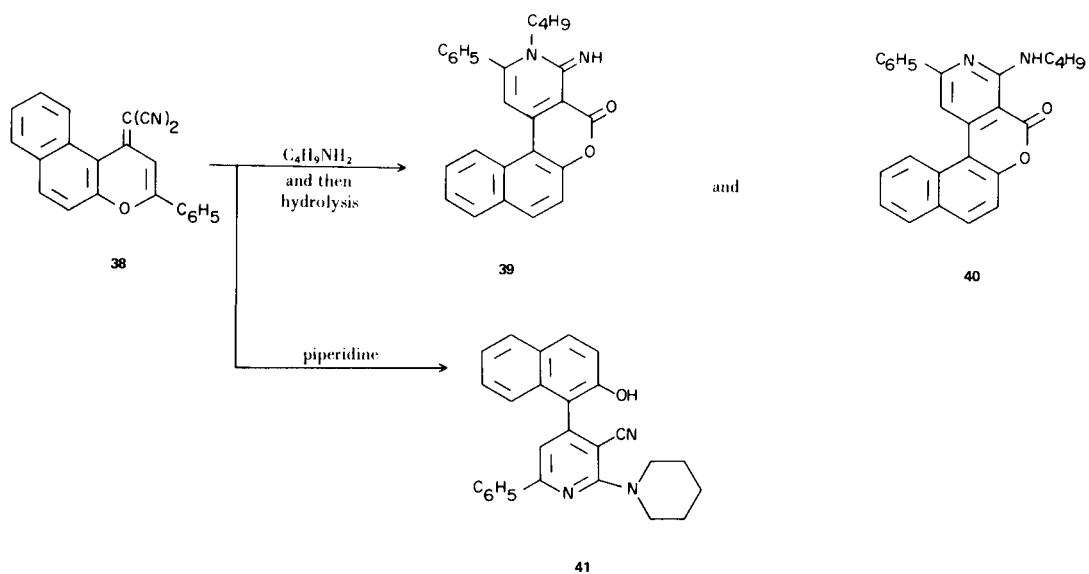
The nmr spectrum in dimethylsulfoxide d₆ (DMSO-d₆) shows absorption for the proton in the 1-position at δ 7.9 (S, 1H), for the -NH₂ at δ 7.8 (S, 2H), and for the aromatic protons at δ 7.25-8.53 ppm (M, 9H).

Anal. Calcd. for C₁₈H₁₂N₂O₂: C, 75.0; H, 4.2; N, 9.7. Found: C, 74.7; H, 4.1; N, 9.4.

Scheme VIII



Scheme IX



4-Amino-5-benzylimino-2-phenyl-5*H*-[1]benzopyrano[3,4-*c*]pyridine (**4**).

A mixture of 1 g. of **3** and 5 ml. of benzylamine was refluxed for 3 hours, cooled, diluted with alcohol, and the solid was collected and crystallized from butyl alcohol to give 1 g. of **4**, m.p. 134-135°.

The λ max ($\epsilon \times 10^{-3}$) are 262 (36.6), 330 (9.0), and 370 $m\mu$ (13.5).

Anal. Calcd. for $C_{25}H_{19}N_3O$: C, 79.6; H, 5.1; N, 11.1. Found: C, 79.4; H, 4.9; N, 11.4.

4-Amino-5-phenylimino-2-phenyl-5*H*-[1]benzopyrano[3,4-*c*]pyridine (**5**).

Compound **5** was prepared from **3** and aniline by the method described for the preparation of **4**. Compound **5** was crystallized from ethoxyethanol and melted at 223-225°.

Anal. Calcd. for $C_{24}H_{17}N_3O$: C, 79.3; H, 4.7; N, 11.6. Found: C, 79.3; H, 4.9; N, 11.7.

4-Amino-2-phenyl-5-(2-phenylhydrazino)-5*H*-[1]benzopyrano[3,4-*c*]pyridine (**6**).

The procedure used for the preparation of **4** was repeated with **3** and phenylhydrazine. Compound **6** was crystallized from pyridine and melted at 215-216°.

The λ max ($\epsilon \times 10^{-3}$) are 242 (47.0), 260 (42.1), 330 (33.2), and 409 $m\mu$ (17.3).

Anal. Calcd. for $C_{24}H_{18}N_4O$: C, 76.2; H, 4.8; N, 14.8. Found: C, 76.4; H, 4.8; N, 15.0.

4-Chloro-2-phenyl-5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-one (**7**).

A solution of 2 g. of **3**, 50 ml. of acetic acid and 10 ml. of concentrated hydrochloric acid was stirred and a solution of 2 g. of sodium nitrite in 5 ml. of water was slowly added. The yellow solid was collected and crystallized from ethoxyethanol, yielding 1.5 g. of **7**, m.p. 227-228°.

The λ max ($\epsilon \times 10^{-3}$) are 267 (34.6) and 327 $m\mu$ (13.5).

Anal. Calcd. for $C_{18}H_{10}ClNO_2$: C, 70.3; H, 3.3; N, 4.6. Found: C, 70.1; H, 3.4; N, 4.5.

2-Phenyl-4,5-dihydro-3*H*-[1]benzopyrano[3,4-*c*]pyridin-4,5-dione (**8**).

(a) The reaction was carried out by the procedure described for **7**, except 5 ml. of sulfuric acid was used in place of the hydrochloric acid, and 1.3 g. of **8** was obtained, m.p. 274-275° (from dimethylformamide).

(b) A mixture of 4.8 g. of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione, 1.3 g. of malononitrile, 3 ml. of diisopropylethylamine, and 100 ml. of acetonitrile was refluxed for 1 hour, cooled, and the solid was collected. The solid was stirred with warm aqueous sodium hydroxide, filtered, the filtrate was neutralized with acetic acid, and the solid was collected and crystallized from nitromethane, giving 1.4 g. of 2-phenyl-5-imino-4,5-dihydro-3*H*-[1]benzopyrano[3,4-*c*]pyridin-4-one, m.p. 255-256°. A solution of 0.5 g. of the latter compound, 15 ml. of acetic acid, and 1 ml. of hydrochloric acid was refluxed 1 hour, diluted with water, cooled, and the solid was collected and crystallized, giving 0.3 g. of **8**, m.p. 273-275°.

The λ max ($\epsilon \times 10^{-3}$) are 337 (15.0), 350 (15.0), and ~ 380 $m\mu$ (7.3).

Anal. Calcd. for $C_{18}H_{11}NO_3$: C, 74.7; H, 3.8; N, 4.9. Found: C, 74.5; H, 4.0; N, 5.2.

2,5-Diphenylpyrido[4,3,2-*mn*][1]benzopyrano[2,3-*d*]pyrimidine (**9**).

A mixture of 1.4 g. of **2**, 1 ml. of benzoyl chloride, and 6 ml. of pyridine was heated for 5 minutes on a steam bath, diluted with water, and the resulting solid was crystallized from dimethylformamide, yielding 1.3 g. of **9**, m.p. 222-223°.

Anal. Calcd. for $C_{25}H_{15}N_3O$: C, 80.4; H, 4.0; N, 11.3. Found: C, 80.2; H, 4.1; N, 11.3.

4-Imino-3-methyl-5-methylimino-2-phenyl-3,4-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (**10**).

A mixture of 2 g. of **1**, 20 ml. of alcohol, and 5 ml. of 40% aqueous methylamine was heated until solution was complete. Excess 70% perchloric acid was added to precipitate the perchlorate salt of **10**, m.p. 237-238°. The free base was obtained by dissolving the perchlorate salt in 10% methanolic potassium hydroxide and diluting the solution with water to give 0.8 g. of **10**, which was crystallized from ligroin (b.p. 100-115°), m.p. 159-160°.

The λ max ($\epsilon \times 10^{-3}$) are 240 (27.1), ~ 245 (25.0), ~ 280 (18.0), 310 (8.4), 330 (9.1), 345 (8.3), and 425 $m\mu$ (7.8).

The nmr spectrum in DMSO- d_6 shows absorption for the methyl protons at δ 3.3 (s, 6H), for the proton in the 1-position at δ 6.2 (s, 1H) and for the aromatic protons at δ 6.9-8.0 ppm (m, 9H).

Anal. Calcd. for $C_{20}H_{17}N_3O$: C, 76.2; H, 5.4; N, 13.3. Found: C, 76.2; H, 5.5; N, 13.5.

3-Butyl-5-butylimino-4-imino-2-phenyl-3,4-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (**11**).

A mixture of 3 g. of **1** and 25 ml. of butylamine was refluxed for 6 hours and evaporated to dryness. The residue was an oil that did not crystallize, but a mass spectrum of the crude product showed that only one material was present and the spectrum was consistent with structure **11**. A sample of the oil was dissolved in alcohol and a small amount of 70% perchloric acid was added. The precipitated perchlorate salt was collected and crystallized from alcohol, m.p. 164-165°.

Anal. Calcd. for $C_{26}H_{30}ClN_3O_5$: C, 62.5; H, 6.1; N, 8.4; Cl, 7.1. Found: C, 62.4; H, 6.3; N, 8.4; Cl, 6.9.

3-Benzyl-5-benzylimino-4-imino-2-phenyl-3,4-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (**12**).

A mixture of 3 g. of **1** and 20 ml. of benzylamine was heated on a steam bath for 3 hours and the excess amine was distilled off under vacuum. The residue was an oil that did not solidify but did show a satisfactory mass spectrum.

4-Imino-3-methyl-2-phenyl-3,4-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-one (**13**).

A solution of 1 g. of **10**, 3 ml. of hydrochloric acid, and 10 ml. of acetic acid was refluxed for 1 hour and neutralized with ammonium hydroxide. The solid was collected and crystallized from alcohol, yielding 0.7 g. of **13**, m.p. 210-211°.

The λ max ($\epsilon \times 10^{-3}$) are 276 (37.0), 325 (9.2), and 435 $m\mu$ (9.2).

Anal. Calcd. for $C_{19}H_{14}N_2O_2$: C, 75.5; H, 4.7; N, 9.3. Found: C, 75.4; H, 4.5; N, 9.5.

3-Butyl-4-imino-2-phenyl-3,4-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-one (**14**).

The method described for the preparation of **13** was repeated with **11** to give 0.65 g. of **14**, m.p. 110-111° (from alcohol).

The λ max ($\epsilon \times 10^{-3}$) are 276 (33.0), 322 (9.3), and 445 $m\mu$ (8.5).

The nmr spectrum in DMSO_d₆ shows absorption for CH₃CH₂CH₂ at δ 0.6-1.75 (M, 7H), for NCH₂ at δ 3.95 (T, 2H), for proton in 1-position at δ 6.47 (S, 1H), aromatic protons at δ 7.2-8.7 (M, 9H), and NH at δ 9.5 (S, 1H) (exchanges with deuterium oxide).

Anal. Calcd. for C₂₂H₂₀N₂O₂: C, 76.7; H, 5.9; N, 8.1. Found: C, 76.4; H, 6.0; N, 7.9.

3-Benzyl-4-imino-2-phenyl-3,4-dihydro-5H-[1]benzopyrano[3,4-c]-pyridin-5-one (**15**).

This compound was prepared from **12** by the method described for **13**, giving 0.6 g. of **15**, m.p. 191-192° (from alcohol).

The λ max ($\epsilon \times 10^{-3}$) are 276 (39.0), 323 (10.0), and 434 m μ (9.5).

Anal. Calcd. for C₂₅H₁₈N₂O₂: C, 79.3; H, 4.8; N, 7.4. Found: C, 79.3; H, 4.9; N, 7.4.

2-Phenyl-4-phenylamino-5-phenylimino-5H-[1]benzopyrano[3,4-c]-pyridine (**16**).

A mixture of 3 g. of **1** and 50 ml. of aniline was refluxed for 3 hours, cooled, and the solid was collected and crystallized from nitromethane, giving 1.7 g. of **16**, m.p. 251-252°.

The λ max ($\epsilon \times 10^{-3}$) are 235 (15.8), 276 (17.7), 289 (18.2), 315 (13.1), and 398 m μ (6.0).

Anal. Calcd. for C₃₀H₂₁N₃O: C, 82.0; H, 4.8; N, 9.6. Found: C, 81.6; H, 4.9; N, 9.8.

4-Butylamino-5-butylimino-2-phenyl-5H-[1]benzopyrano[3,4-c]-pyridine (**17**).

A mixture of 3 g. of **1** and 25 ml. of butylamine was heated for 8 hours in a bomb at 150°, cooled, and the solid was removed by filtration and crystallized from alcohol, yielding 1.6 g. of **17**, m.p. 95-96°.

The λ max ($\epsilon \times 10^{-3}$) are 262 (42.6), ~280 (28.0), 302 (18.1), 333 (7.3), and 392 m μ (13.3).

The nmr spectrum in DMSO_d₆ shows absorption for C-CH₃ at δ 0.73 (M, 6H), for CCH₂CH₂Me at δ 1.33 (M, 8H), for NCH₂Pr at δ 3.28 (M, 4H), for aromatic protons at δ 6.94-8.06 (M, 10H), and for NH at δ 9.9 (M, 1H). The addition of deuterium oxide changes the NCH₂ absorption to a distorted triplet.

Anal. Calcd. for C₂₆H₂₉N₃O: C, 78.2; H, 7.3; N, 10.5. Found: C, 78.4; H, 7.4; N, 10.6.

2-Phenyl-4-phenylamino-5H-[1]benzopyrano[3,4-c]pyridin-5-one (**18**).

A mixture of 1 g. of **16**, 3 ml. of hydrochloric acid, and 10 ml. of acetic acid was refluxed for 1 hour, diluted with 5 ml. of water and chilled. The solid was collected and crystallized from acetic acid, m.p. 224-225°.

The λ max ($\epsilon \times 10^{-3}$) are 259 (30.0), ~280 (32.0), 298 (33.0), and 395 m μ (10.0).

Anal. Calcd. for C₂₄H₁₆N₂O₂: C, 79.1; H, 4.4; N, 7.7. Found: C, 79.0; H, 4.6; N, 7.6.

4-Butylamino-2-phenyl-5H-[1]benzopyrano[3,4-c]pyridin-5-one (**19**).

Compound **16** was hydrolyzed by the procedure described for the preparation of **13**, yielding 0.7 g. of **19**, m.p. 110-111° (from alcohol).

The λ max ($\epsilon \times 10^{-3}$) are 255 (38.0), 276 (40.0), ~309 (4.0), and 395 m μ (17.0).

The nmr spectrum in DMSO_d₆ shows absorption for CH₃CH₂CH₂ at δ 0.83 (M, 7H), for NCH₂ at δ 3.6 (M, 2H), and

for the aromatic protons at δ 7.3-8.7 ppm (M, 10H). The addition of deuterium oxide causes NCH₂ to change to a distorted triplet.

Anal. Calcd. for C₂₂H₂₀N₂O₂: C, 76.6; H, 5.9; N, 8.1. Found: C, 76.4; H, 6.0; N, 7.8.

4-Benzylamino-2-phenyl-5H-[1]benzopyrano[3,4-c]pyridin-5-one (**20**).

(a) A mixture of 2 g. of **1** and 15 ml. of benzylamine was refluxed for 1 hour, cooled, and mixed with dilute aqueous acetic acid. The liquid was decanted from a gum, which was dissolved in a mixture of 20 ml. of acetic acid and 3 ml. of hydrochloric acid. The solution was refluxed for 1 hour, evaporated to dryness, and the residue was dissolved in a small amount of boiling pyridine and chilled. The solid was collected and boiled with 100 ml. of alcohol. The mixture was filtered hot to remove some insoluble material, which was crude **20**. The alcohol filtrate was chilled to give 0.9 g. of **3**, m.p. 210-211°. The alcohol-insoluble material was crystallized from ethoxyethanol, giving 0.3 g. of **20**, m.p. 212-213°.

The λ max ($\epsilon \times 10^{-3}$) are ~240 (18.0), 257 (28.5), 276 (30.0), ~315 (2.7), and 387 m μ (11.5).

(b) A mixture of 1 g. of **15** and 15 ml. of benzylamine was refluxed for 2 hours, diluted with aqueous acetic acid, and the solid that formed was crystallized from ethoxyethanol, giving 0.7 g. of **20**, m.p. 212-213°.

Anal. Calcd. for C₂₅H₁₈N₂O₂: C, 79.3; H, 4.8; N, 7.4. Found: C, 79.1; H, 5.0; N, 7.2.

2-Phenyl-4-piperidino-5H-[1]benzopyrano[3,4-c]pyridin-5-one (**21**).

A mixture of 3 g. of **1** and 50 ml. of piperidine was refluxed for 6 hours, evaporated to dryness, and the residue was crystallized from aqueous acetic acid, giving 2.2 g. of **21**, m.p. 225-226°.

The λ max ($\epsilon \times 10^{-3}$) are 211 (27.0), 262 (18.8), 283 (17.5), ~296 (15.3), and 395 m μ (5.0).

Anal. Calcd. for C₂₃H₂₀N₂O₂: C, 77.5; H, 5.7; N, 7.9. Found: C, 77.2; H, 5.5; N, 7.9.

3-Cyano-2-methoxy-4-(2-hydroxyphenyl)-6-phenylpyridine (**22**).

A mixture of 3 g. of **1**, 3 g. of sodium methoxide and 100 ml. of methyl alcohol was refluxed for 6 hours, cooled, filtered, and the filtrate was neutralized with acetic acid. The solid was collected and crystallized from nitromethane, yielding 1.4 g. of **22**, m.p. 230-231°.

The λ max ($\epsilon \times 10^{-3}$) are 220 (20.0), 262 (16.5), ~325 (11.4), and 352 m μ (19.2).

The infrared spectrum shows absorption for a cyano and a hydroxy group.

The nmr spectrum in DMSO_d₆ shows absorption for OCH₃ at δ 4.12 (S, 3H), for the aromatic protons at δ 6.93-8.1 (M, 10H), and for the OH at δ 11.6 ppm (broad S, 1H). The hydroxide proton exchanges with deuterium oxide.

Anal. Calcd. for C₁₉H₁₄N₂O₂: C, 75.5; H, 4.7; N, 9.3. Found: C, 75.2; H, 4.6; N, 9.6.

3-Cyano-4-(2-hydroxyphenyl)-6-phenyl-2-pyridone (**23**).

(a) A mixture of 2.1 g. of **22**, 5 ml. of hydrochloric acid, and 15 ml. of acetic acid was refluxed for 1 hour, cooled, and the solid was collected and crystallized from pyridine, yielding 1.7 g. of **23**, m.p. 350-351°.

(b) A mixture of 2.3 g. of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione and 1 g. of cyanoacetamide in 10 ml. of alcohol and 3 ml. of diisopropylethylamine was refluxed for 5 hours.

Water was added to the clear solution, followed by acetic acid. The precipitate was collected and crystallized from pyridine giving 2.1 g. of **23**, m.p. 350-351°.

Anal. Calcd. for C₁₈H₁₂N₂O₂: C, 75.0; H, 4.2; N, 9.7. Found: C, 75.3; H, 4.5; N, 9.9.

4-(Dicyanomethylene-2-phenyl-4*H*-naphtho[1,2-*b*]pyran (**24**).

(a) A mixture of 15 g. of 2-phenylnaphtho[1,2-*b*]pyran-4-one, 5 g. of malononitrile and 60 ml. of acetic anhydride was refluxed for 1/2 hour, chilled, and the solid was collected and crystallized from ethoxyethanol, giving 6 g. of **24**, m.p. 246-247°.

(b) A mixture of 50 g. of 2-phenylnaphtho[1,2-*b*]pyran-4-one, 18 g. of malononitrile, and 100 ml. of phosphorus oxychloride was heated on a steam bath for 2 hours, cooled, poured into methyl alcohol, and the solid was collected and crystallized, giving 50 g. of **24**, m.p. 245-246°.

Anal. Calcd. for C₂₂H₁₂N₂O: C, 82.5; H, 3.8; N, 8.8. Found: C, 82.4; H, 3.6; N, 8.9.

4-Amino-5-imino-2-phenyl-5*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridine (**25**).

A mixture of 3 g. of **24** and ammonium hydroxide was allowed to react by the procedure described for **2**, giving 2 g. of **25**, m.p. 218-219° from ethoxyethanol.

The λ max ($\epsilon \times 10^{-3}$) are 254 (70.0) and 353 μ (16.9).

Anal. Calcd. for C₂₂H₁₅N₃O: C, 78.3; H, 4.5; N, 12.5. Found: C, 77.9; H, 4.8; N, 12.3.

3-Butyl-5-butylimino-4-imino-2-phenyl-4,5-dihydro-3*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridine (**26**).

A mixture of 2 g. of **24** and 25 ml. of butylamine was refluxed for 4 hours and evaporated to dryness. The residue was an amber gum which did not crystallize. The gum was dissolved in 10 ml. of alcohol and 2 ml. of 70% perchloric acid was added. The solid was collected and crystallized from alcohol, giving 1.5 g. of the perchlorate salt of **26**, m.p. 179-181°.

Anal. Calcd. for C₃₀H₃₂ClN₃O₅: C, 65.5; H, 5.9; N, 7.6. Found: C, 65.2; H, 5.6; N, 7.3.

3-Benzyl-5-benzylimino-4-imino-2-phenyl-4,5-dihydro-3*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridine (**27**).

A mixture of 2 g. of **24** and 10 ml. of benzylamine was heated on a steam bath for 2 hours, cooled, diluted with alcohol, and the solid was crystallized from butyl alcohol, giving 1.9 g. of **27**, m.p. 205-206°.

The λ max ($\epsilon \times 10^{-3}$) are 275 (38.0), 288 (32.0), 360 (10.0), 380 (12.4), 445 (4.7), and \sim 470 μ (**2.5**).

Anal. Calcd. for C₃₆H₂₇N₃O: C, 83.5; H, 5.3; N, 8.1. Found: C, 83.6; H, 5.1; N, 8.3.

4-Amino-2-phenyl-5*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridin-5-one (**28**).

Compound **28** was prepared from **25** by the procedure described for **3**. The m.p. of **28** was 270-271° (from pyridine).

Anal. Calcd. for C₂₂H₁₄N₂O₂: C, 78.1; H, 4.2; N, 8.3. Found: C, 77.8; H, 4.3; N, 8.5.

3-Butyl-4-imino-2-phenyl-4,5-dihydro-3*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridin-5-one (**29**).

The procedure described for **3** was used to prepare compound **29** from **26**. The yield of **29** was 89% and the m.p. was 192-193° (from alcohol).

The λ max ($\epsilon \times 10^{-3}$) are 268 (49.0), 302 (19.0), 318 (21.0), 368 (12.0), and 445 μ (8.7).

The nmr spectrum in deuterochloroform shows absorption for CH₂CH₂CH₃ at δ 1.37 (M, 7H), for NCH₂Pr at δ 3.98 (T, 2H), for the proton in the 1-position at δ 5.94 (S, 1H), for the aromatic protons at δ 7.65-8.47 (M, 11H), and for NH at δ 9.1 ppm (broad S, 1H).

Anal. Calcd. for C₂₆H₂₂N₂O₂: C, 79.2; H, 5.6; N, 7.1. Found: C, 79.0; H, 5.8; N, 7.3.

3-Benzyl-4-imino-2-phenyl-4,5-dihydro-3*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridin-5-one (**30**).

Compound **30** was prepared from **27** by the procedure described for **3**. The yield of **30** was 86% and the m.p. was 269-270° (from ethoxyethanol).

Anal. Calcd. for C₂₉H₂₀N₂O₂: C, 81.3; H, 4.7; N, 6.5. Found: C, 81.0; H, 4.9; N, 6.8.

4-Butylamino-5-butylimino-2-phenyl-5*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridine (**31**).

This compound was prepared from 3 g. of **24** and 25 ml. of butylamine by the procedure described for **17**. The yield of **31** was 2.2 g. and the m.p. was 142-143° (from nitromethane).

The λ max ($\epsilon \times 10^{-3}$) are 220 (50.0), 266 (66.0), 360 (12.5), and 400 μ (10.0).

Anal. Calcd. for C₃₀H₃₁N₃O: C, 80.2; H, 6.9; N, 9.4. Found: C, 80.1; H, 6.9; N, 9.7.

4-Amino-4-benzylamino-2-phenyl-5*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridine (**32**).

A mixture of 2 g. of **24** and 10 ml. of benzylamine was refluxed for 8 hours, cooled, diluted with alcohol, and the solid was collected and crystallized from pyridine, yielding 1.4 g. of **32**, m.p. 239-240°.

The λ max ($\epsilon \times 10^{-3}$) are 268 (54.5), 351 (16.0), and 365 μ (17.3).

Anal. Calcd. for C₂₉H₂₁N₃O: C, 81.5; H, 5.0; N, 9.8. Found: C, 81.1; H, 5.1; N, 10.1.

Hydrolysis of a sample of **32** with acetic and hydrochloric acids gave **28**.

4-Butylamino-2-phenyl-5*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridin-5-one (**33**).

Compound **31** was hydrolyzed by the procedure described for **3**, giving a 91% yield of **33**, m.p. 154-155° (from ethoxyethanol).

The nmr spectrum in DMSO-d₆ shows absorption for CH₂CH₂CH₃ at δ 1.0 (M, 7H), for NCH₂Pr at δ 3.4 (M, 2H), for proton in 1-position δ 7.18 (S, 1H), and for aromatic protons 7.27-8.58 ppm (M, 11H).

The λ max (chloroform) ($\epsilon \times 10^{-3}$) are 253 (54.0) and 405 μ (17.5).

Anal. Calcd. for C₂₆H₂₂N₂O₂: C, 79.2; H, 5.6; N, 7.1. Found: C, 79.6; H, 5.9; N, 7.1.

2-Phenyl-4-piperidino-5*H*-naphtho[2',1':5,6]pyrano[3,4-*c*]pyridin-5-one (**34**).

Compound **34** was prepared in 56% yield from **24** and piperidine by the procedure described for **21**. The m.p. was 193-194° (from acetic acid).

The λ max ($\epsilon \times 10^{-3}$) are 262 (68.0), \sim 305 (26.0), 355 (7.5), and 395 μ (12.5).

Anal. Calcd. for C₂₇H₂₂N₂O₂: C, 79.8; H, 5.5; N, 6.9. Found: C, 79.8; H, 5.4; N, 7.0.

7-Amino-8-cyano-6-imino-9-phenyl-6*H*-benzo[*d*]naphtho[1,2-*b*]pyran (**35**).

A mixture of 3.2 g. of **24** and 1 g. of cyanoacetamide was

dissolved in 25 ml. of hot pyridine, 10 ml. of 10% methanolic potassium hydroxide was added, and the mixture was heated on a steam bath for 1 hour. The solid was collected, washed with alcohol, and crystallized from pyridine, giving 3 g. of **35**, m.p. 278-279°.

The λ max ($\epsilon \times 10^{-3}$) are 272 (63.0), 312 (5.6), 325 (4.9), and 392 $m\mu$ (24.2).

Essentially the same results were obtained when cyanoacetanilide was substituted for the cyanoacetamide.

Anal. Calcd. for $C_{24}H_{15}N_3O$: C, 79.8; H, 4.2; N, 11.6. Found: C, 79.3; H, 4.4; N, 11.3.

4-Cyano-2,5-diphenylbenzo[*de*]naphtho[2',1':5,6]pyrano[2,3-*d*]pyrimidine (**36**).

A mixture of 1 g. of **35**, 1 ml. of benzoyl chloride, and 15 ml. of pyridine was heated on a steam bath for 2 hours, diluted with water, and the solid was collected and crystallized from dimethylformamide, giving 1 g. of **36**, m.p. 307-309°.

The λ max ($\epsilon \times 10^{-3}$) are 280 (84.2), 370 (14.8), 387 (25.0), and 407 $m\mu$ (26.4).

Anal. Calcd. for $C_{31}H_{17}N_3O$: C, 83.2; H, 3.8; N, 9.4. Found: C, 82.9; H, 4.1; N, 9.7.

7-Amino-8-cyano-9-phenyl-6*H*-benzo[*d*]naphtho[1,2-*b*]pyran (**37**).

A mixture of 0.5 g. of **35**, 2 ml. of hydrochloric acid, and 20 ml. of acetic acid was refluxed for 1 hour, cooled, and the solid was collected and crystallized from pyridine, giving 0.3 g. of **37**, m.p. 265-266°.

The λ max ($\epsilon \times 10^{-3}$) are 257 (69.4), 305 (11.4), 318 (10.0), ~380 (27.0), and 398 $m\mu$ (29.0).

Anal. Calcd. for $C_{24}H_{14}N_2O_2$: C, 79.6; H, 3.9; N, 7.7. Found: C, 79.6; H, 4.1; N, 8.0.

1-Dicyanomethylene-3-phenyl-1*H*-naphtho[2,1-*b*]pyran (**38**).

This compound was prepared by the procedure used for **24** and melted at 267-268° (from pyridine).

The λ max ($\epsilon \times 10^{-3}$) are 241 (40.5), 286 (11.2), 359 (23.0), and 400 $m\mu$ (17.4).

Anal. Calcd. for $C_{22}H_{12}N_2O$: C, 82.5; H, 3.8; N, 8.8. Found: C, 82.6; H, 3.6; N, 9.0.

3-Butyl-4,5-dihydro-4-imino-2-phenyl-naphtho[1',2':5,6]pyrano[3,4-*c*]pyridin-5-one (**39**).

A mixture of 3 g. of **38** and 25 ml. of butylamine was refluxed for 4 hours, evaporated to dryness, the residue was dissolved in hot alcohol, and 2 ml. of 70% perchloric acid was added to the alcohol solution. The precipitate was collected and added to 20 ml. of acetic acid and 5 ml. of hydrochloric acid. The solution was refluxed for 1 hour, evaporated to dryness, and the residue was dissolved in hot pyridine. The product was precipitated by the addition of ammonium hydroxide to the pyridine solution and was crystallized from pyridine, giving 1.2 g. of **39**.

The λ max ($\epsilon \times 10^{-3}$) are 322 (19.0), 360 (14.2), 374 (14.0), and 455 $m\mu$ (7.5).

Anal. Calcd. for $C_{26}H_{22}N_2O_2$: C, 79.2; H, 5.6; N, 7.1. Found: C, 79.2; H, 5.3; N, 6.8.

4-Butylamino-2-phenyl-5*H*-naphtho[1',2':5,6]pyrano[3,4-*c*]pyridin-5-one (**40**).

The procedure described for the preparation of **39** was repeated, except that the crude residue (obtained after the butylamine was evaporated) was hydrolyzed directly, rather than first isolating a perchlorate salt of the intermediate. The crude hydrolysis product was crystallized from alcohol, yielding 1 g. of **40**, m.p. 117-118°.

The λ max ($\epsilon \times 10^{-3}$) are 293 (30.7), ~315 (19.5), 352 (11.0), and 405 $m\mu$ (16.2).

The nmr spectrum in DMSO- d_6 shows absorption at δ 0.78-1.21 for $CH_3CH_2CH_2$ (M, 7H), at δ 3.4 for NCH_2Pr (M, 2H), and the aromatic protons at δ 7.18-8.58 ppm (M, 12H). The multiplet for the NCH_2Pr changes to a triplet on addition of deuterium oxide.

Anal. Calcd. for $C_{26}H_{22}N_2O_2$: C, 79.2; H, 5.6; N, 7.1. Found: C, 79.0; H, 5.9; N, 6.9.

3-Cyano-4-(2-hydroxy-1-naphthyl)-6-phenyl-2-piperidinopyridine (**41**).

A mixture of 3 g. of **38** and 50 ml. of piperidine was refluxed for 14 hours, evaporated to dryness, and the residue was crystallized from acetic acid and then nitromethane, giving 2.4 g. of **41**, m.p. 305-306°.

The λ max ($\epsilon \times 10^{-3}$) are 228 (82.6), 277 (34.8), ~338 (7.8), and 362 $m\mu$ (9.0).

The infrared spectrum shows absorption for cyano and hydroxy groups.

Anal. Calcd. for $C_{27}H_{23}N_3O$: C, 80.0; H, 5.7; N, 10.4. Found: C, 79.7; H, 5.8; N, 10.5.

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